Editors' comments and author responses

Impaired Ca^{2+} signaling indicates disturbed mitochondrial function in fibroblasts from patients with sporadic and familial ALS

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Editors: Cristiane Cecatto, Erich Gnaiger

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Manuscript edited 2022-11-04: *Only major points included.*

Editors

Abstract; L 138; L 173; L 221: Calcium capacity must be defined explicitly, not restricted to showing the data in Figure 1. In L 173 you use the term 'matrix calcium capacity' – what is the difference? In L 221: You use the term 'calcium retention capacity' with reference to Figure 1 – what is the difference?

Authors

We agree with the comment. The 'calcium retention capacity' term has been fixed throughout the text.

Editors

L 12; L 16: Define the meaning of 'intracellular systems' – or better avoid this term and provide the information directly.

Authors

Corrected as

L 12: "The mitochondrial Ca^{2+} overload-associated energy deficit affects the activity of key Ca^{2+} transporting mechanisms….."

L 16: "The crosstalk between these transport systems is tightly controlled….."

Editors

L 51, Table 1: Is reporting of mean and SD supported by normal data distribution, or should medians be reported?

Authors

The mean and SD are supported by normal distribution. The Median and Range are provided in addition. Thanks to the notice, a few mistyped digits were recognized. Fixed.

Editors

It is advisable to replace levels of significance (*, **, ***) by simply stating the actual *p*-values. – See MitoPedia: BEC
https://www.bioblast.at/index.php/Statistical_significance

Authors

It is hard to disagree with the trend of statistical data presentation and interpretation. We would follow the recommendation; however, the study was performed such a long time ago, so our attempts in opening the files give us a problem. We would like to ask to accept the current presentation as an exemption.

Editors

L 136: Does the cytosolic Ca^{2+} peak depend on the amount of free (or total accumulated?) Ca^{2+} in the mitochondria? In any case, the Ca^{2+} peak corresponds to the mitochondrial retention capacity only at identical mitochondrial densities, if mitochondrial calcium retention capacity is defined per mitochondrial marker rather than per mitochondrial population in a cell.

Authors

Ca^{2+} peak depends on the amount of free Ca^{2+} as the signal of fluorescent probe rises upon binding with ionized Ca^{2+} only.

We assume that the mitochondrial markers if determined would correspond to the mitochondria population, as there is no way of determining the mitochondrial density, either in suspension of isolated mitochondria or cells, other than via mitochondrial markers/proteins. The experimental setting puts the limitation of determining the mitochondrial markers effectively, the accurate cell count was employed instead.

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Editors

L 203: "Retaining the accumulated Ca^{2+} in mitochondria as much important as its sequestration and depends on the inner mitochondrial membrane potential." Can delta pH be ignored?

Authors

Agreed and accept suggested sentence: "Retaining the accumulated Ca^{2+} in mitochondria is as important as its sequestration and depends on the mitochondrial membrane potential and ΔpH, i.e., on the protonmotive force."